Remarks

Previously withdrawn claims 16-32 and 37-39, and previously pending claims 6 and 36 have been canceled without prejudice to their being asserted in this or any continuation or divisional application. New claims 40-54 have been added. Claims 1, 5, 9, 34 and 35 have been amended. Claims 1-5, 7-15, 34-35 and 40-54 are pending in this application. No new matter has been added.

Applicant notes the rejection of the claims under 35 U.S.C. §112. Applicant respectfully traverses these rejections for the reasons discussed below. Notwithstanding, applicant has entered new claims 40-47 based on original claims 9-15 and 34-35 incorporating language which the Examiner has indicated is enabled and has adequate written description. As there is no prior art asserted against original claims 9-15 and 34-35, and applicant has incorporated language which avoids the §112 rejection, applicant respectfully maintains that new claims 40-47 are in condition for allowance.

Additionally, applicant has entered new claims 48-54 based on original claims 1-5 and 7-8 incorporating language which the Examiner has indicated is enabled and has adequate written description. Claims 1-8 have been rejected by the Examiner as anticipated. For the reasons discussed below, applicant respectfully maintains that claims 1-8 are not anticipated. Thus, since the applicant has incorporated language which avoids the §112 rejection, applicant respectfully maintains that new claims 48-54 are in condition for allowance.

Priority

The Examiner has rejected Applicant's claim for priority to U.S. Patent Applications Nos. 09/835,784, 09/549,926, 09/120,264, 09/087,210 and 08/864,357 because the Examiner believes that these applications do not provide support for methods of identifying

compounds that bind to fibronectin type III (fnIII) polypeptides or that compete for binding with uteroglobin. Applicant respectfully traverses the Examiner's rejection.

Applicant notes that the current application is a continuation-in-part of U.S. Application No. 09/835,784 which is a continuation-in-part of application no. 09/549,926, which is a continuation-in-part of application no. 09/120,264, which is a continuation-in-part of application no. 09/087,210 which is a continuation-in-part of application no. 08/864,357 and that a proper claim for priority under §120, referencing these continuations-in-part, was made in the this application at the time for filing.

Specification

Applicant thanks the Examiner for pointing out certain typographical errors relating to trademarks used in the application. To the extent that these trademarks require generic descriptions and/or capitalization, applicant has amended the specification of the instant application to provide such description. No new matter has been added by these amendments.

35 U.S.C. §112

Omitted step

The Examiner has rejected claims 1-15 and 34-36 under §112, second paragraph, for omitting the step of "determining whether a compound inhibits a fibronectin mediated process." Applicant respectfully traverses the Examiner's rejection. Applicant notes that "determining (e.g. identifying) whether a compound inhibits a fibronectin mediated process" is the general goal of the claim and is accomplished by following the particular method claimed, e.g. "determining whether a candidate compound binds a fnIII polypeptide" or "inhibits or disrupts binding between a fnIII polypeptide and a uteroglobin-like compound." Where a candidate compound accomplishes binding, inhibition or disruption, as claimed, it has the

property of inhibiting fibronectin-mediated processes. Thus by determining binding, inhibition or disruption one would automatically determine whether or not a candidate compound inhibits fibronectin-mediated processes.

Definiteness

The Examiner has rejected claims 1-7, 9-14 and 34-36 under §112, second paragraph, as indefinite because the specification does not define "fibronectin-mediated processes." Applicant respectfully traverses the §112, second paragraph indefiniteness rejection.

Applicant first notes that the Examiner has concluded that the specification does teach that fnIII domains are involved in fibronectin-dependent cell adhesion, polymerization, deposition and fibronectin-fibronectin interactions. Applicant notes that these are examples of fibronectin-mediated processes.

Applicant respectfully points out that the specification does teach fibronectin-mediated processes generally. For example at par. 159-160 the specification describes fibronectin-mediated processes as:

> Therefore, the present invention provides methods of identifying compounds capable of inhibiting fibronectin-mediated processes. In a preferred embodiment, the method comprises determining whether a candidate compound binds a fibronectin Type III polypeptide. Whether the compound binds the fibronectin Type III polypeptide may be determined in a competitive binding assay.
>
> In another preferred embodiment, the method comprises determining whether a candidate compound inhibits or disrupts binding between a fibronectin Type III polypeptide and a uteroglobin-like compound. The determination of whether a candidate compound inhibits or disrupts binding between a fibronectin Type III polypeptide and a uteroglobin-like compound may be carried out in a competitive binding assay.

Thus fibronectin-mediated processes, as claimed, are those processes which can be inhibited by binding to the fnIII polypeptide and those processes which can be inhibited by inhibiting or

disrupting binding between a fnIII polypeptide and a uteroglobin-like compound. Applicant further points out that the original claims of the application also support this definition. Thus applicant respectfully maintains that "fibronectin-mediated process" is adequately defined by the specification and therefore not indefinite.

Enablement

The Examiner has rejected claims 1-15 and 34-36 under §112, first paragraph, as not enabling for methods of identifying compounds capable of inhibiting processes involving all fnIII polypeptides. Applicant respectfully traverses the §112, first paragraph enablement rejection.

Applicant first notes that the Examiner has concluded that the specification does enable determining whether a compound binds fibronectin or superfibronectin and determining whether the compound inhibits cell adhesion. Applicant notes that these are examples of processes involving fnIII polypeptides.

The Examiner asserts that not all the polypeptides encompassed by the claims are involved in fibronectin mediated processes. Applicant respectfully maintains that any polypeptide encompassed by the claims is necessarily involved in a fibronectin-mediated process because fibronectin-mediated processes, as claimed, are those processes which can be inhibited by binding to the fnIII polypeptide and those processes which can be inhibited by inhibiting or disrupting binding between a fnIII polypeptide and a uteroglobin-like compound. Thus applicant respectfully maintains that methods of identifying compounds which inhibit processes involving fnIII polypeptides is adequately enabled by the specification because one of ordinary skill would know that fibronectin-mediated processes involve polypeptides which can be inhibited by binding to the fnIII domain and those processes which can be inhibited by inhibiting or

disrupting binding between a fnIII domain and a uteroglobin-like compound.

The Examiner has rejected claims 1-15 and 34-36 under §112, first paragraph, as not enabling for methods of determining whether a compound competitively binds fibronectin or superfibronectin in the presence of any other 4-helix bundle polypeptide. Applicant respectfully traverses the §112, first paragraph enablement rejection.

Applicant first notes that the Examiner has concluded that the specification does enable determining whether a compound competitively binds fibronectin or superfibronectin. Solely to speed prosecution, applicants have hereinabove amended claims 5 and 34-35 to recite uteroglobin instead of 4-helix bundle polypeptide.

35 U.S.C. 102(b)

The Examiner has rejected claims 1-8 as anticipated under 35 U.S.C. 102(b) by Sipes *et al.*, (1993 J. Cell Biol. 121(2): 469-477) ("Sipes"), U.S. Patent No. 5,491,130 ("'130 patent"), and U.S. Patent No. 5,817,750 ("'750 patent"). The Examiner has also rejected claims 1 and 7 as anticipated under 35 U.S.C. 102(b) by Shimuzu *et al.*, (1997, *Biol. Pharm. Bull.* 20(12): 1219-1223).

The Examiner contends that Sipes anticipates claims 1-8 because it teaches direct binding assays and competitive binding assays that identify peptides that bind to fibronectin, peptides which inhibit fibronectin binding to gelatin and fibronectin-mediated cell adhesion to a gelatin or collagen matrix. The Examiner states that Sipes is silent as to whether the peptide identified by his method would interfere with uteroglobin binding, but concludes that it would be an inherent feature of the peptide because the peptide interferes with fibronectin-mediated cell adhesion.

The Examiner asserts that the '130 patent anticipates claims 1-8 because it teaches

direct binding and competitive binding assays wherein peptides are screened for their ability to bind fibronectin and inhibit fibronectin-mediated cell adhesion. The Examiner states that the '130 patent is silent as to whether the peptide identified by this method would interfere with uteroglobin binding, but concludes that it would be an inherent feature of the peptide because the peptide interferes with fibronectin-mediated cell adhesion.

The Examiner maintains that the '750 patent anticipates claims 1-8 because it teaches a method to isolate peptides which interact with fibronectin, binding competition, and assays for peptide inhibition of the cell attachment function of integrins. The Examiner states that the '750 patent is silent as to whether the peptide identified by this method would interfere with uteroglobin binding, but concludes that it would be an inherent feature of the peptide because the peptide interferes with fibronectin-mediated cell adhesion.

Lastly, the Examiner asserts that Shimizu anticipates claims 1 and 7 because it teaches a standardized assay system for fibronectin activity using fibronectin-mediated cell adhesion.

In response, applicant respectfully traverses the Examiner's §102(b) rejections. Applicants maintain that presently pending claims 1-8 are not anticipated by Sipes, the '130 patent or the '750 patent and that claims 1 and 7 are not anticipated by Shimuzu.

Well established Federal Circuit precedent confirms that in to order establish anticipation by a reference, that reference must describe each and every limitation of the claim. Applicants respectfully submit that the cited references do not describe each and every limitation of the respective rejected claims.

As amended, independent claim 1 reads:

> A method of identifying compounds capable of inhibiting fibronectin-mediated processes, comprising determining whether a

candidate compound binds a fibronectin Type III polypeptide
wherein said candidate compound is a fragment of uteroglobin.

Applicants respectfully submit that Sipes, the '130 patent, the '750 patent and Shimizu do not disclose a method of identifying compounds wherein the candidate compound is a fragment of uteroglobin. Sipes merely describes binding assays which identify human thrombospondin-1 based peptides which bind to fibronectin. (Sipes at p. 471). The '130 patent also merely describes human thrombospondin-1 based peptides which bind to fibronectin and the '750 patent merely describes binding of synthetic cyclic peptide fragments which mimic a binding site of an integrin. ('130 patent col. 8; '750 patent col. 11-13). Finally, Shimizu merely describes an assay system for determining whether cells bind to fibronectin molecules which are immobilized on a plastic microtiter well. Shimizu does not provide a method for identifying fragments of uteroglobin which bind a fibronectin Type III polypeptide.

With respect to the Examiner's inherency contentions, the Examiner has provided no support for her hypothesis that because peptides from the Sipes, '130 patent, and '750 patent apparently interfere with fibronectin-mediated cell adhesion, that they would inherently interfere with uteroglobin binding. Applicant respectfully points out that Federal Circuit case law dictates that inherency requires that "the disclosure of the prior art is sufficient to show that the natural result flowing from the operation as taught in the prior art would result in the claimed product." *Smithkline Beecham v. Apotex Corp.*, slip op. at 20, (Fed. Cir. April 8, 2005).

Applicant submits that the Examiner has made no showing that a peptide which interferes with fibronectin-mediated cell adhesion would naturally result in interference with uteroglobin binding. For example, it is equally possible that a peptide which interferes with fibronectin-mediated cell adhesion would not interfere with uteroglobin binding because fibronectin has other binding domains besides the domain to which uteroglobin binds. (*e.g.* the

gelatin binding domain of the '130 patent).

. . .

For at least the reasons set forth above, pending claims 1-5, 7-15, 34-35 and 40-54 are urged as being in condition for allowance. Prompt allowance is therefore respectfully requested. If any issues remain outstanding, applicants invite the Examiner to discuss the same at a telephone interview with the undersigned.

No additional fees, except the fee for a three month extension, are believed to be necessary in connection with the filing of this Amendment. However, if any additional fees are required, the Commissioner is hereby authorized to charge such fee(s) to Deposit Account No. 05-0765.

Respectfully submitted,

Dated: September 19, 2005

Barry Evans, Esq.
Reg. No. 22,802
Henry J. Cittone, Esq.
Reg. No. 57,206
KRAMER LEVIN NAFTALIS & FRANKEL LLP
1177 Avenue of the Americas
New York, New York 10036
(212) 715-9100 (telephone)
(212) 715-8000 (facsimile)